

Notice of Allowability

Application No.

09/255,963

Examiner

Sumesh Kaushal Ph.D.

Applicant(s)

MA, PETER X.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 01/02/04.
2. ☒ The allowed claim(s) is/are 1-20,23,25-30,33-38 and 40-55.
3. ☒ The drawings filed on 23 February 1999 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

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EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Julia Church Dierker on 03/19/04.

The application has been amended as follows:

IN THE CLAIMS

Claim 22 and 32 were canceled

Claims 1, 2, 11, 23 and 34 were amended as below:

1. *(Currently amended)*. A method comprising the steps of:

mixing an alginate salt and a source of calcium ions to provide a mixture; adding a calcium releasing compound to the mixture to provide a three-dimensional crosslinked hydrogel system; and

selectively controlling shrinking, swelling or maintaining of the hydrogel system by varying a calcium ion concentration of a separate medium into which the hydrogel system is introduced,

wherein the hydrogel system swells at calcium ion concentrations in the medium between about 0.0005 M and about 0.0010 M; wherein the hydrogel system shrinks at a calcium ion concentration in the medium of about 0.0040 M; and wherein the hydrogel system remains substantially the same size at calcium ion concentrations in the medium between about 0.0020 M and about 0.0030 M.

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2. (*Currently amended*) The method of Claim 1, further comprising the step of culturing the three-dimensional crosslinked hydrogel system in a medium for growing cells *in vitro*.

11. (*Currently amended*) A method for tissue engineering *in vitro*, the method comprising the steps of:

mixing cells, an alginate salt and a source of calcium ions to provide a mixture;
adding a calcium releasing compound to the mixture to provide a crosslinked hydrogel;
selectively controlling shrinking, swelling or maintaining of the crosslinked hydrogel by varying a calcium ion concentration of a separate medium into which the crosslinked hydrogel is introduced; and

culturing the crosslinked hydrogel in the medium to provide a three-dimensional crosslinked hydrogel/cell system for growing the cells *in vitro*,

wherein the hydrogel system swells at calcium ion concentrations in the medium between about 0.0005 M and about 0.0010 M; wherein the hydrogel system shrinks at a calcium ion concentration in the medium of about 0.0040 M; and wherein the hydrogel system remains substantially the same size at calcium ion concentrations in the medium between about 0.0020 M and about 0.0030 M.

23. (*Currently amended*) A method for preparing a three-dimensional hydrogel system, the method comprising the steps of:

adding a calcium-releasing compound to a mixture of at least one hydrophilic polymer comprising an alginate salt and a source of calcium cations to provide a three-dimensional crosslinked hydrogel system; and

selectively controlling shrinking, swelling or maintaining of the hydrogel system by varying a calcium ion concentration of a separate medium into which the hydrogel system is introduced,

wherein the hydrogel system swells at calcium ion concentrations in the medium between about 0.0005 M and about 0.0010 M; wherein the hydrogel system shrinks at a calcium ion concentration in the medium of about 0.0040 M; and wherein the hydrogel system remains

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substantially the same size at calcium ion concentrations in the medium between about 0.0020 M and about 0.0030 M.

34. (*Currently amended*) A three-dimensional crosslinked hydrogel composition, consisting essentially of:

at least one hydrophilic polymer comprising an alginate salt;
a source of calcium cations;
a calcium-releasing compound, whereby a mixture of the at least one hydrophilic polymer, the source of calcium cations and the calcium-releasing compound forms the crosslinked hydrogel composition; and

a separate culture medium into which the hydrogel composition is introduced, the culture medium having a predetermined calcium ion concentration, wherein the predetermined calcium ion concentration determines the shrinking, swelling or maintaining of the crosslinked hydrogel composition,

wherein the hydrogel system swells at calcium ion concentrations in the medium between about 0.0005 M and about 0.0010 M; wherein the hydrogel system shrinks at a calcium ion concentration in the medium of about 0.0040 M; and wherein the hydrogel system remains substantially the same size at calcium ion concentrations in the medium between about 0.0020 M and about 0.0030 M.

IN THE SPECIFICATION

Page 7, line 5, "Figure 1" was replaced with – Figure 1a-1b – before "is a graph".

Page 7, line 7, "Figure 2" was replaced with – Figure 2a-2b – before "is a graph".

Page 7, line 9, "Figure 3" was replaced with – Figure 3a-3b – before "is a graph".

Page 7, line 11, "Figure 4" was replaced with – Figure 4a-4b – before "is a graph".

Page 7, line 13, "Figure 5" was replaced with – Figure 5a-5b – before "is a graph".

Page 7, line 15, "Figure 6" was replaced with – Figure 6a-6b – before "is a graph".

REASONS FOR ALLOWANCE

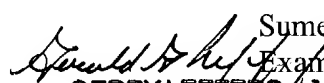
The following is an examiner's statement of reasons for allowance:

Claims 1-20, 23, 25-30, 33-38 and 40-55 are free of prior art of record. The prior art does not teach or suggest a three-dimensional crosslinked hydrogel composition for tissue engineering, wherein the shrinking, swelling or maintaining of the hydrogel system is selectively controlled by varying a calcium ion concentration of a separate medium into which the hydrogel system is introduced, and wherein the hydrogel system as claimed swells at calcium ion concentrations in the medium between about 0.0005 M and about 0.0010 M. The hydrogel system shrinks at a calcium ion concentration in the medium of about 0.0040 M; and wherein the hydrogel system remains substantially the same size at calcium ion concentrations in the medium between about 0.0020 M and about 0.0030 M.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Sumesh Kaushal
Examiner Art Unit 1636
GERRY LEFFERS
PRIMARY EXAMINER